

Document made available under the Patent Cooperation Treaty (PCT)

International application number: PCT/US05/004421

International filing date: 14 February 2005 (14.02.2005)

Document type: Certified copy of priority document

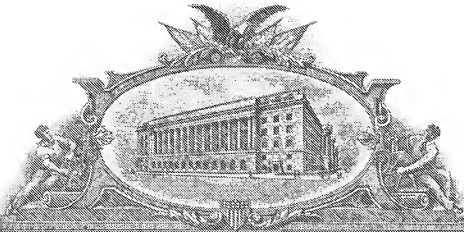
Document details: Country/Office: US
Number: 60/544,905
Filing date: 13 February 2004 (13.02.2004)

Date of receipt at the International Bureau: 27 June 2005 (27.06.2005)

Remark: Priority document submitted or transmitted to the International Bureau in compliance with Rule 17.1(a) or (b)



World Intellectual Property Organization (WIPO) - Geneva, Switzerland
Organisation Mondiale de la Propriété Intellectuelle (OMPI) - Genève, Suisse



THE UNITED STATES OF AMERICA

TO ALL TO WHOM THESE PRESENTS SHALL COME:

UNITED STATES DEPARTMENT OF COMMERCE

United States Patent and Trademark Office

June 15, 2005

THIS IS TO CERTIFY THAT ANNEXED HERETO IS A TRUE COPY FROM THE RECORDS OF THE UNITED STATES PATENT AND TRADEMARK OFFICE OF THOSE PAPERS OF THE BELOW IDENTIFIED PATENT APPLICATION THAT MET THE REQUIREMENTS TO BE GRANTED A FILING DATE.

APPLICATION NUMBER: 60/544,905

FILING DATE: *February 13, 2004*

RELATED PCT APPLICATION NUMBER: PCT/US05/04421



Certified by

Under Secretary of Commerce
for Intellectual Property
and Director of the United States
Patent and Trademark Office

PROVISIONAL APPLICATION FOR PATENT COVER SHEET

This is a request for filing a PROVISIONAL APPLICATION FOR PATENT under 37 CFR 1.53(c).

Express Mail Label No. EV372403634US

INVENTOR(S)

Given Name (first and middle [if any])	Family Name or Surname	Residence (City and either State or Foreign Country)
Joseph M. Jason P.	DeSimone Rolland	Durham, NC Durham, NC

Additional inventors are being named on the _____ separately numbered sheets attached hereto

TITLE OF THE INVENTION (500 characters max)

FUNCTIONAL MATERIALS AND NOVEL METHODS FOR THE FABRICATION OF MICROFLUIDIC DEVICES

Direct all correspondence to:

CORRESPONDENCE ADDRESS

☒ Customer Number: 25297

OR

☐ Firm or
Individual Name

Address

Address

City

State

ZIP

Country

Telephone

Fax

ENCLOSED APPLICATION PARTS (check all that apply)

☒ Specification Number of Pages 21

☐

CD(s), Number _____

☐ Drawing(s) Number of Sheets _____

☐

Other (specify) _____

☐ Application Data Sheet. See 37 CFR 1.76

METHOD OF PAYMENT OF FILING FEES FOR THIS PROVISIONAL APPLICATION FOR PATENT

☒ Applicant claims small entity status. See 37 CFR 1.27.

☐ A check or money order is enclosed to cover the filing fees.

☒ The Director is hereby authorized to charge filing fees or credit any overpayment to Deposit Account Number: 50-0426

☐ Payment by credit card. Form PTO-2038 is attached.

FILING FEE
Amount (\$)

80.00

The invention was made by an agency of the United States Government or under a contract with an agency of the United States Government.

☒ No.

☐ Yes, the name of the U.S. Government agency and the Government contract number are: _____

Respectfully submitted,

[Page 1 of 1]

Date 02/13/04

SIGNATURE Arlas A. Taylor

REGISTRATION NO. 39,395

TYPED or PRINTED NAME Arlas A. Taylor, Jr.

(If appropriate)

Docket Number: 421/96 PROV

TELEPHONE 919-493-8000

USE ONLY FOR FILING A PROVISIONAL APPLICATION FOR PATENT

This collection of information is required by 37 CFR 1.51. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 8 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Mail Stop Provisional Application, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

JENKINS
WILSON
& TAYLOR

patent attorneys

February 13, 2004

RICHARD E. JENKINS

JEFFREY L. WILSON

ARLES A. TAYLOR, JR.

GREGORY A. HUNT

E. ERIC MILLS

BENTLEY J. OLIVE

MICHAEL J. CROWLEY

CHRIS PERKINS, PH.D.

JAMES DALY IV, PH.D.

JEFFREY CHILDERS, PH.D.

OF COUNSEL
SOROJINI BISWAS

"Express Mail" mailing number.: EV372403634US

Date of Deposit: February 13, 2004

I hereby certify that this correspondence is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 C.F.R. 1.10 on the date indicated above and is addressed to the Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.


Patty Wilson

Mail Stop Provisional Application
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Re: U.S. Provisional Patent Application for
FUNCTIONAL MATERIALS AND NOVEL METHODS FOR
THE FABRICATION OF MICROFLUIDIC DEVICES
Our Ref. No. 421/96 PROV

Sir:

Please find enclosed the following:

1. Provisional Application Cover Sheet (1 pg.) in duplicate;
2. U.S. Provisional Patent Application (21 pgs.);
3. A return-receipt postcard to be returned to our offices with the U.S. Patent and Trademark Office date stamp thereon; and
4. A Certificate of Express Mail No.: EV372403638US.

Please contact our offices if there are any questions.

Commissioner for Patents
February 13, 2004
Page 2

The Commissioner is hereby authorized to charge any fees associated with the filing of this correspondence to Deposit Account Number 50-0426.

Respectfully submitted,

JENKINS, WILSON & TAYLOR, P.A.

A handwritten signature in dark ink, appearing to read "Arles A. Taylor, Jr.", is positioned above the printed name.

Arles A. Taylor, Jr.
Registration No. 39,395

AAT/ptw

Enclosures

Customer No: 25297

UNITED STATES PROVISIONAL PATENT APPLICATION

**FUNCTIONAL MATERIALS AND NOVEL METHODS FOR THE FABRICATION
OF MICROFLUIDIC DEVICES**

Co-Inventors: Joseph M. DeSimone, Ph.D.
 Durham, North Carolina, USA

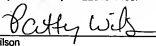
 Jason Rolland
 Durham, North Carolina, USA

Assignee: The University of North Carolina at Chapel Hill

Entity: Small

JENKINS, WILSON & TAYLOR, P.A.
Suite 1400, University Tower
3100 Tower Boulevard
Durham, North Carolina 27707
Telephone: 919-493-8000
Facsimile: 919-419-0383

"Express Mail" mailing number.: EV372403638US
 Date of Deposit: February 13, 2004
 I hereby certify that this correspondence is being deposited with
 the United States Postal Service "Express Mail Post Office to
 Addressee" service under 37 C.F.R. 1.10 on the date indicated
 above and is addressed to the Commissioner for Patents, P. O.
 Box 1450, Alexandria, VA 22313-1450.


 Patty Wilson

FUNCTIONAL MATERIALS AND NOVEL METHODS FOR THE FABRICATION OF MICROFLUIDIC DEVICES

TECHNICAL FIELD

5

The presently disclosed subject matter relates to functional materials for use in fabricating microfluidic devices. More particularly, the presently disclosed subject matter relates to functional materials for use in attaching biological and other "switchable" molecules to the interior surfaces of microfluidic channels.

10

The presently disclosed subject matter also relates to methods for fabricating microfluidic devices. More particularly, the presently disclosed subject matter relates to a fabrication method using degradable polymers as scaffolds for producing complex, two-dimensional (2-D) and three-dimensional (3-D) microfluidic networks. A method of adhering two-dimensional and three-dimensional microfluidic networks to a substrate also is disclosed.

15

SUMMARY

The presently disclosed subject matter relates to materials and methods for use in fabricating microfluidic devices. The materials and methods described herein exhibit several advantages over the current state of the art. First, the materials described herein offer chemical functionality to the interior surface of microfluidic channels, which allows for the attachment of biopolymer and other small organic "switchable" molecules that can affect channel hydrophobicity or reactivity. Second, the molding method described herein uses scaffolds of degradable polymers to form channels inside a microfluidic device. The ability to rapidly mold complex three-dimensional structures inside a device using a scaffolding process is not known in the art. The molding method disclosed

20

25

herein allows for complex three-dimensional networks of channels to be formed in one step. As such, the molding process described herein is simpler than methods known in the art for fabricating multilayer devices. Third, the adhesion method described herein is simpler than the partial bonding methods known in the art. The adhesion method also allows for bonding to other materials, such as poly(dimethyl siloxane) (PDMS) networks.

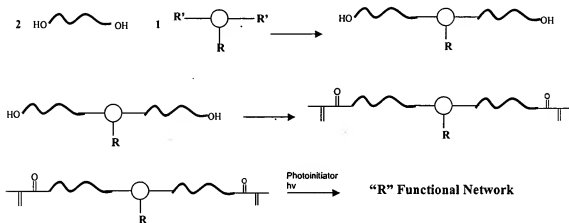
The functional microfluidic devices described by the presently disclosed subject matter advance the field of microfluidic devices in several regards. First, by attaching biomolecules to the interior surfaces of the microfluidic channels, combinatorial peptide synthesis or rapid screenings of enzyme-protein interactions can be envisioned. Second, if the microfluidic channels are lined with catalysts, rapid catalyst screening is possible. Third, if switchable organic molecules are introduced into the microfluidic channels, devices that have both hydrophilic and hydrophobic channels can be fabricated.

STATEMENT OF THE INVENTION

The presently disclosed subject matter relates to materials and methods for functionalizing the channels in a microfluidic device. In some embodiments, such functionalization includes, but is not limited to, the synthesis and/or attachment of peptides and other natural polymers to the interior surface of a channel in a microfluidic device. The presently disclosed subject matter can be applied to microfluidic devices, such as those described by Rolland, J., et al., J. Am. Chem. Soc., 2004, ASAP Article (Feb. 6, 2004), the disclosure of which is incorporated herein by reference in its entirety. Briefly, such microfluidic devices are made from photocurable perfluoropolyether materials that pour like silicones and cure into durable, highly fluorinated, chemical resistant elastomers. See DeSimone et al., pending U.S. Provisional Patent Application Serial No. 60/531,531; DeSimone et al., pending U.S. Provisional Patent Application Serial No. 60/538,878; and DeSimone et al., pending U.S. Provisional Patent Application Serial No. 60/538,706, which are incorporated herein by reference in

their entirety. The materials and methods described herein are not limited to devices made of these fluoroelastomers, but are applicable to devices made from any material, e.g., poly(dimethyl siloxane) (PDMS) and polyurethane.

In some embodiments, the presently disclosed subject matter adds functionality to a microfluidic channel by adding a chemical "linker" moiety to the elastomer itself. In some embodiments, a functional group is added along the backbone of the precursor material. An example of this method is illustrated in Scheme 1.



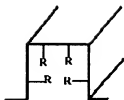
Scheme 1. Synthesis of functional materials for microfluidic devices.

In some embodiments, the precursor material comprises a macromolecule containing hydroxyl functional groups. In some embodiments, the hydroxyl functional groups comprise diol functional groups. In some embodiments, two or more of the diol functional groups are connected through a trifunctional "linker" molecule. In some embodiments, the trifunctional linker molecule has two functional groups, R and R' . In some embodiments, the R' group reacts with the hydroxyl groups of the macromolecule. In some embodiments, the R group provides the desired functionality to the interior surface of the microfluidic channel. In some embodiments, the R' group is selected from the group including, but not limited to, acid chloride, isocyanate, halogen, and ester

moieties. In some embodiments, the R group is selected from one of, but not limited to, protected amines and protected alcohols. In some embodiments, the macromolecule diol is functionalized with polymerizable methacrylate groups. In some embodiments, the functionalized macromolecule diol is cured and/or
5 molded by a photochemical process as described by Rolland, J., et al., J. Am. Chem. Soc., 2004, ASAP Article (Feb. 6, 2004), the disclosure of which is incorporated herein by reference in its entirety.

In some embodiments, the method comprises adding a functional monomer to an uncured precursor material. In some embodiments, the method
10 further comprises incorporating the functional monomer into the network by a curing step. In some embodiments, the precursor material comprises a fluoropolymer. In some embodiments, the functional monomer comprises a highly fluorinated monomer. In some embodiments, the highly fluorinated monomer comprises perfluoro ethyl vinyl ether (EVE). In some embodiments,
15 the precursor material comprises a poly(dimethyl siloxane) (PDMS) elastomer. In some embodiments, the precursor material comprises a polyurethane elastomer. In some embodiments, the functional monomer is selected from the group consisting of functional styrenes, methacrylates, and acrylates.

In some embodiments, the method comprises binding a small molecule to
20 the interior surface of a microfluidic channel. In such embodiments, once bound, the small molecule can serve a variety of functions. In some embodiments, the small molecule functions as a cleavable group, which when activated, can change the polarity of the channel and hence the wettability of the channel. In some embodiments, the small molecule functions as a binding site. In some
25 embodiments, the small molecule functions as a binding site for one of a catalyst, a drug, a substrate for a drug, an analyte, and a sensor. In some embodiments, the small molecule functions as a reactive functional group. In some embodiments, the reactive functional group is reacted to yield a Zwitterion. In some embodiments, the Zwitterion provides a polar, ionic channel. A schematic
30 of a functionalized channel is provided in Scheme 2.



Scheme 2. Schematic of a microfluidic channel with "R" functionalization.

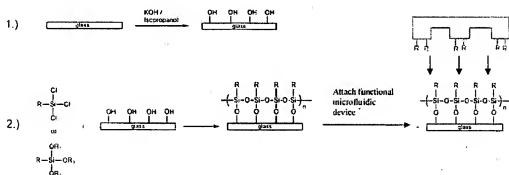
5 The presently disclosed subject matter also provides a method of adhering two-dimensional and three-dimensional microfluidic networks to a substrate. The adhesion of the two layers in a multi-dimensional microfluidic device presents a significant challenge. Proper adhesion is required to achieve valve actuation without destroying the device. Unger et al. have shown that adhesion is achieved in a two-component system, such as PDMS, by adding an excess of one component to one layer and an excess of the other component to the layer to which it is bonding. See Unger et al., Science, 288, 113-116 (2000). When dealing with single component systems, such as those described by the presently disclosed subject matter, adhesion is a challenge. Adhesion can be achieved by selecting a cure time that balances feature integrity with proper adhesion between the layers.

10 In the presently disclosed subject matter, adhesion is achieved by adding a two-component fluorinated system to the precursor. In some embodiments, adhesion is achieved by adding a diisocyanate macromolecule to one layer and a diol macromolecule to the other. In some embodiments, these additives are bonded post-cure in a similar manner as is done with PDMS systems.

20 In some embodiments, the adhesion method further comprises adhering a microfluidic device to a substrate. In some embodiments, the substrate is a glass substrate. In some embodiments, adhering the microfluidic device to a substrate allows the microfluidic device to be operated at high flow pressures.

25 In some embodiments, the adhesion method comprises using methoxysilanes to add functionality to a glass surface. In some embodiments,

the adhesion method further comprises attaching methacrylate groups to a surface that can react post cure to form residual groups in the network. In some embodiments, the method comprises attaching other functional groups to a surface and using the macromolecule additive approach outlined above. An example of this approach is provided in Scheme 3. In some embodiments, the functional groups of this method are selected from one of an isocyanate and an alcohol.

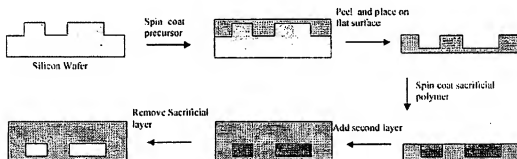


Scheme 3. Adhesion of functional microfluidic devices to glass substrates.

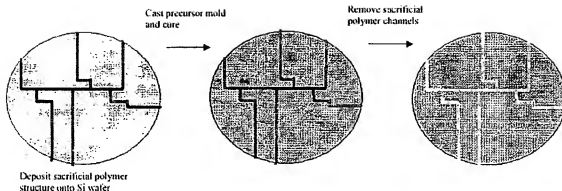
The presently disclosed subject matter also describes the use of sacrificial polymer layers for the use in fabricating channels and complex structures in a microfluidic device. Importantly, the compatibility of the materials and devices disclosed herein with organic solvents provides the capability to utilize sacrificial polymer structures in microfluidic devices. These materials protect the channels from being filled in when another layer of elastomer is cast on top. In some embodiments, the material is spin-coated to the depth of the channels. In some embodiments, the material is a degradable material. In some embodiments, the material is removed from the channel. In some embodiments, the material is degraded. In some embodiments, the material is removed or degraded by one of heat, light, and dissolution. In some embodiments, the materials for use in the sacrificial channels are selected from the group consisting of polyolefin sulfones, cellulose fibers, polylactones, and polyelectrolytes. In some embodiments, the materials for use in the sacrificial channels are selected from a material that can be degraded or dissolved away. In some embodiments, the material is selected

from the group consisting of salts, water-soluble polymers, and solvent-soluble polymers.

In addition to simple channels, the presently disclosed subject matter also provides for the fabrication of multiple complex structures that can be "injection molded" or fabricated ahead of time and embedded into the material and removed as described above. In some embodiments, a structure is made of a sacrificial polymer. In some embodiments, the polymer is surrounded by a liquid precursor. In some embodiments, the method further comprises curing the polymer/liquid precursor composition. In some embodiments, the sacrificial polymer structure comprises a two-dimensional structure. In some embodiments, the sacrificial polymer structure comprises a three-dimensional structure. In some embodiments, the method further comprises the step of degrading or dissolving the polymer to yield channels within the devices. An example of this process is provided in Scheme 4. The fabrication of complex structures in microfluidic devices is further illustrated in Scheme 5.



Scheme 4. Fabrication of channels using sacrificial polymer layers.



Scheme 5. Fabrication of complex structures in microfluidic devices.

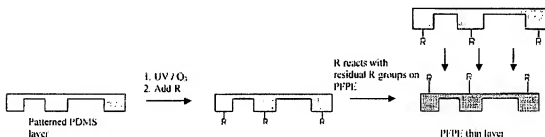
5 The presently disclosed subject matter also provides materials and methods for fabricating a hybrid poly(dimethyl siloxane) (PDMS)/perfluoropolyether (PFPE) microfluidic device. One disadvantage of PFPE materials is their high cost. The presently disclosed subject matter provides a hybrid device that uses solvent-resistant materials, such as PFPE, in the thin fluid layer, while the air channels and the bulk of the device are made of PDMS or another less expensive material.

10 In some embodiments, the layer in the microfluidic device upon which fluids are introduced comprises a layer of a solvent resistant material of a thickness range. In some embodiments, the solvent resistant material comprises PFPE. In some embodiments, the thickness range comprises about 10 to 30 μm . In some embodiments, the thickness comprises about 20 μm . In some embodiments, the channels above this layer are used for air actuation.

15 In some embodiments, the method of fabricating the device comprises adhering the PDMS layer to the PFPE layer. In some embodiments, the method comprises introducing an allyl-functional PFPE macromonomer that will not react during the free radical cure. In some embodiments, the method further comprises reacting the allyl-functional PFPE macromonomer post-cure with silane groups on the cured PDMS network through a hydrosilation reaction.

20 In some embodiments, the method comprises introducing surface functionality to the PDMS network by using an oxygen plasma. In some

embodiments, the method comprises introducing a functional group to the patterned surface of the PDMS block. In some embodiments, the functional group is a methacrylate group. In some embodiments, the method further comprises binding the PFPE network to the PDMS block by reacting the functional groups of the PDMS block with residual functional groups on the PFPE layer. In some embodiments, the method further comprises binding the PFPE network to the PDMS block through a curing process. An example of a method of fabricating a hybrid PDMS/PFPE microfluidic device is provided in Scheme 6.



Scheme 6. Fabrication of a hybrid PDMS/PFPE microfluidic device.

The presently disclosed subject matter also provides for the use of functionalized PFPE networks as gas separation membranes. In some embodiments, the functionalized PFPE network is used as a gas separation membrane to separate gases selected from the group consisting of CO₂, methane, hydrogen, CO, CFCs, CFC alternatives, organics, nitrogen, methane, H₂S, amines, fluorocarbons, fluoroolefins, and O₂. In some embodiments, the functionalized PFPE network is used to separate gases in a water purification process. In some embodiments, the gas separation membrane comprises a stand-alone film. In some embodiments, the gas separation membrane comprises a composite film. In some embodiments, the gas separation membrane comprises co-monomers. In some embodiments, the co-monomers are utilized to regulate the permeability properties of the gas separation membrane. The mechanical strength and durability of such membranes can be finely tuned by adding composite fillers, such as silica particles and others, to the membrane. Accordingly, in some embodiments, the membrane further

comprises a composite filler. In some embodiments, the composite filler comprises silica particles.

CONFIDENTIAL

THE UNIVERSITY OF NORTH CAROLINA AT CHAPEL HILL

REPORT OF INVENTION

RECEIVED

FEB 10 2004

BY: _____

1. DISCLOSING PARTIES* :

1 (and primary contact person)

2

Name: Joseph DeSimone
Rank/Professional: _____
Affiliation: William R. Kenan Jr. Distinguished Professor of Chemistry
Campus Address: Venable Hall, CB#3290 Chapel Hill, NC 27599
Campus Phone No. 919-962-2166
Campus FAX No. 919-962-5467
E-Mail Address: desimone@unc.edu
Citizenship: United States of America
Home Address: _____
Home Phone No. 919-933-2513

Jason Rolland
graduate student
Venable Hall, CB#3290 Chapel Hill, NC 27599
919-962-1346
919-962-5467
rolland@email.unc.edu
United States of America
102 Hollow Oak Dr., Durham, NC 27713
919-619-1409

**We ask for "disclosing parties" rather than "inventors" because an inventor is one who contributes to the conception of an invention as that invention is subsequently defined by one or more patent claims; therefore the final determination on inventorship must wait until such time as a patent application is filed.*

***If any of the inventors were employed by other institutions while the invention was being made, please include the name, address and phone number of that institution.*

[FOR ADDITIONAL DISCLOSING PARTIES, PLEASE USE THE SAME FORMAT AS ABOVE AND ATTACH AS AN ADDENDUM AT THE END OF THIS REPORT]

Pursuant to the Patent Policy of The University of North Carolina at Chapel Hill, I/we hereby disclose details about the following invention:

a. TITLE OF INVENTION:

Functional Materials and Novel Methods for the Fabrication of Microfluidic Devices

3. DATE OF INVENTION: [Indicate actual or approximate dates.]

Earliest conception*: 1-15-04
Experimentation Period: 1-15-04 - present
Reduction to Practice**: has not been reduced to practice

Are experimental data validating the invention or prototypes of the invention available?

Data has been collected on the synthesis, characterization, and photocuring of these perfluoropolyethers. We have also synthesized working microfluidic devices from such materials.¹

**Conception means the formation, in the mind of the inventor(s), of a definite and permanent idea of the complete and operative invention as claimed, as it is thereafter to be applied in practice.*

***If the invention has not been reduced to practice, please so indicate.*

OTD 04-007

OTD
CONFIDENTIAL

4. DESCRIPTION OF INVENTION:

Describe the invention in detail. Attach additional pages as necessary.

Functional Materials and Novel Methods for Fabrication of Microfluidic Devices Jason P. Rolland and Joseph M. DeSimone

The invention described herein relates to novel functional materials for the fabrication of microfluidic devices as well as novel methods for the generation of those devices. The invention stems from previous work published by our group in which we describe the fabrication of the first microfluidic devices compatible with organic solvents.¹ These devices are made from photocurable perfluoropolyether materials that pour like silicones and cure into durable, highly fluorinated chemically resistant elastomers. The methods described herein are not limited to devices made of these fluoroelastomers but are applicable to devices made from any material (eg. PDMS, polyurethane, etc...)

1. Functional materials for binding small molecules, peptides, biological molecules, and other polymers.

An area in microfluidics that remains to be explored is the functionalization of select channels in the device. This includes the synthesis and/or attachment of peptides and other natural polymers. We add functionality to microfluidic channels by adding chemical "linker" moieties to the elastomer itself. This can be done in 2 ways: One such way is to add these functional groups along the backbone of the precursor material. An example of this is shown in Figure 1. In this illustration, we begin with a diol functional macromolecule. Two (or more) of these chains can be connected through a trifunctional "linker" molecule which has two functionalities that will react with the alcohol (R') and one group (R) that provides the desired functionality to the inside of the microfluidic channel. Examples of R' include but are not limited to acid chloride, isocyanate, halogen, and ester moieties. Examples of R include but are not limited to protected amines and protected alcohols. The second reaction in this scheme shows the functionalization of this macro diol with polymerizable methacrylate groups. This final molecule can be cured / molded photochemically in the same manner as reported previously.¹

A second, simpler method would be to add functional monomers to the uncured precursor materials and hence incorporate them into the network upon curing. For fluoropolymer precursor materials these functional monomers will include highly fluorinated monomers such as EVE. In other systems such as PDMS or polyurethane elastomers, traditional functional styrenes, methacrylates and acrylates will be easily blended and incorporated into the precursor material.

The functionalization of microfluidic channels is not limited to the binding of natural and synthetic polymers. Herein we also can bind small molecules to the inside of the channel. Once bound, these molecules can serve a variety of functions including but not limited to: 1) a cleavable group which when activated can change the polarity of channel and hence the wettability, 2) groups that could act as binding sites for catalysts, drugs, substrates for drugs, analytes of all types, especially for sensors, etc. 3) functional groups which could subsequently be reacted to yield Zwitterions and thus very polar, ionic channels. A cartoon illustration of what a functionalized channel would look like is shown in Figure 2.

OTD 04-09-07

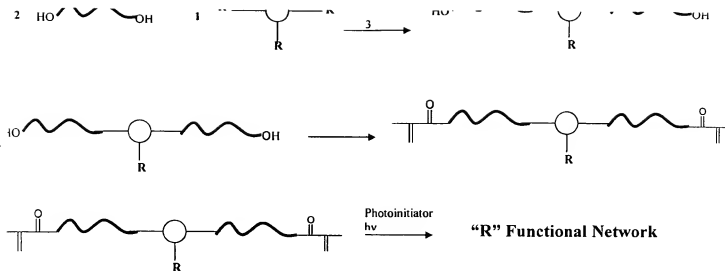


Figure 1. Synthesis of functional materials for microfluidic devices

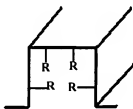


Figure 2. Cartoon illustration of a microfluidic channel with "R" functionalization

II. Additives for adhesive promotion between layers of multi-dimensional microfluidic devices as well as adhesion to surfaces.

A significant challenge exists in so called multi-dimensional microfluidic devices is the adhesion of the two layers. Proper adhesion is required to achieve valve actuation without destroying the device. Quake et al¹ have shown that in a two-component system such as PDMS, this adhesion is easily achieved by adding excess of one component to one layer and excess of the other component to the layer it is bonding to. When dealing with single component systems such as those developed by our group, adhesion becomes a delicate challenge by carefully finding a cure time that balances feature integrity with proper adhesion between layers. Here we can solve this adhesion issue by simply adding a two component fluorinated system to the precursors. For example, one can add a diisocyanate macromolecule to one layer and a diol macromolecule to the other. These groups could be bonded post cure in a similar manner as is done with PDMS systems.

A related issue is proper adhesion of the working device to a glass substrate. This ensures that high flow pressures can be tolerated. We can readily achieve this by using methoxysilanes to add functionality to a glass surface. Examples of this include but are not limited to: 1) Attaching methacrylate groups to a surface that can react post cure to residual groups in the network, 2) attaching other functional groups such as isocyanates or alcohols to a surface and using the macromolecular additive approach outlined above. A schematic of this approach is illustrated in Figure 3.

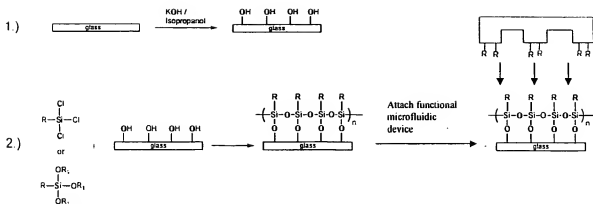


Figure 3. Adhesion of functional microfluidic devices to glass substrates

III. Use of sacrificial polymer layers in the fabrication of channels and more complex structures.

The compatibility of our materials and devices with organic solvents offers exciting opportunities in the realm of sacrificial polymer structures in microfluidic devices. Our materials allow for degradable materials to be spin-coated to the depth of the channels. These materials can then protect the channels from being filled in when another layer of elastomer is cast on top. The material can then be removed/degraded by heat, light, or dissolution. Materials for use in the sacrificial channels include but are not limited to: polyolefin sulfones, cellulose fibers, polylactones, polyelectrolytes, and almost any other material that can be degraded or dissolved away including salts, polymers of different solubility characteristics like water soluble materials or solvent soluble materials.

In addition to simple channels, we also can fabricate multiple complex structures that can be "injection molded" or fabricated ahead of time and embedded into our material and removed as described above. In this approach, a 2-D or 3-D complex structure made of the desired sacrificial polymer is surrounded with the liquid precursor and cured. Subsequent degradation/dissolution yields channels within the device. While the diagram in Figure 4 suggests a 2-dimensional structure, we wish to emphasize that this method could easily be applied to 3-dimensional structures as well.

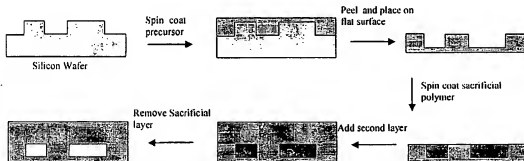


Figure 4. Fabrication of channels using sacrificial polymer layers

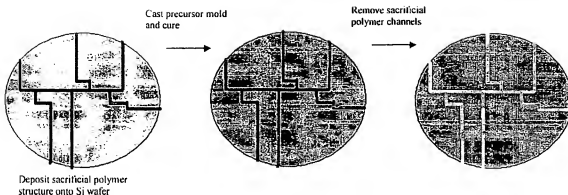


Figure 5. Fabrication of complex structures in microfluidic devices

IV. PDMS-PFPE composite devices.

A possible disadvantage of the PFPE materials is their high cost. On many devices, a thin (20 μm) layer is used as the layer in which fluids are introduced. The channels above this layer are only used for air actuation. Thus, we claim a hybrid device that uses our solvent-resistant materials in the thin fluid layer while the air channels and the bulk of the device made of PDMS or another cheaper material. The crucial component of this will be the adhesion of the PDMS layer to the PFPE layer. This can be accomplished several ways, 1) introduce an allyl-functional PFPE macromonomer that will not react during the free radical cure, but could be reacted post-cure with excess silane groups on the cured PDMS network through a hydrosilation reaction. 2) Using an oxygen-plasma, surface functionality can be introduced to PDMS networks. One can imagine introducing methacrylate groups to the patterned surface of the PDMS block which could be used to bind to the PFPE network that is cured through such functional groups. This concept is illustrated in Figure 5.

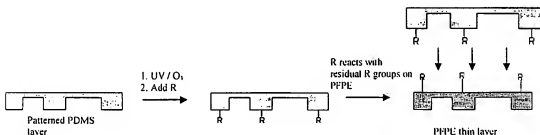


Figure 6. Illustration of hybrid PDMS-PFPE microfluidic device fabrication

References

- 1.) Rolland, J.; Van Dam, M.; Schorzman, D.; Quake, S.R.; DeSimone, J.M. *J. Am. Chem. Soc.* **2004**, *ASAP*.
- 2.) Unger, M. A.; Chou, H. P.; Thorsen, T.; Scherer, A.; Quake, S. R. *Science*. **2000**, *288*, 113-6.

- a. Write a brief descriptive abstract of the invention without disclosing any confidential information. This may be used for marketing purposes.

The invention described involves novel functional materials which will allow the attachment of biological and other "switchable" molecules to the inside of microfluidic channels. We also describe a novel fabrication method that uses degradable

OTD 04 0067

polymers as scaffolds for the production of complex, 2-D and 3-D microfluidic networks. Other ideas disclosed involve novel adhesion techniques of these devices to glass and other materials.

- b. Expand on novel and unusual features which distinguish this invention from present technology. What problems does the invention solve or what advantages does it possess?

These novel materials and techniques exhibit several advantages over current systems:

- 1) They offer chemical functionality to the inside of microfluidic channels which allows for the attachment of biopolymer and other small organic "switchable" molecules that can affect channel hydrophobicity or reactivity.
- 2) We disclose novel molding techniques that use scaffolds of degradable polymers to form channels inside microfluidic devices. This is a much simpler method than others used to generate multilayer devices. It allows for complex 3-D networks of channels to be formed in one step.
- 3) The adhesion methods described are simpler and more elegant than partial bonding techniques reported previously. They also allow for bonding to other materials such as PDMS networks.

- c. Comment on possible uses for the invention. In addition to immediate applications, are there other uses that might be realized in the future?

These functional microfluidic devices will take the field to new levels. By attaching biomolecules to the insides of the channels one can imagine combinatorial peptide synthesis or rapid screenings of enzyme-protein interactions. If the channels are lined with catalysts, rapid catalyst screening will be possible. If switchable organic molecules are introduced, devices that have both hydrophilic and hydrophobic channels could be fabricated.

The ability to rapidly mold complex 3D structures inside a device using scaffolding techniques is unprecedented in the literature. Such structures will allow for and elegance in microfluidic capabilities not yet seen.

- d. Describe any disadvantages or limitations of the invention. Can they be overcome? How?

No such limitations are evident at this time.

- e. Are there known inventions or products that would compete with this one? Please describe, including information on relevant patents and publications, if available.

No such techniques are reported in the literature.

- g. Are there any prior patent applications or patents by the inventor(s) related to this invention? If so, list the serial number(s) and filing date(s).

OTD 04.06.07

[USE ADDITIONAL SHEETS IF NECESSARY AND ATTACH DESCRIPTIVE MATERIALS
THAT MAY PROMOTE A BETTER UNDERSTANDING OF THE INVENTION]

OTD _____

CONFIDENTIAL

5. PREVIOUS AND/OR FUTURE DISCLOSURES OF THE INVENTION:

- a. Indicate details of any full or partial prior disclosure of this invention such as: manuscript, article, report, grant application, thesis, abstract, poster, demonstration, sales catalog, news release, internal memorandum, oral presentation, or discussion with an industry representative. SPECIFY DATE AND ATTACH COPIES OF ANY WRITTEN DISCLOSURE.

There has been no disclosure of the above invention.

- b. Have there been any changes in the invention since publication? If so, describe.

- c. Describe in detail any plans for future disclosure of this invention. This may include submission of a manuscript, article, report, grant application, thesis, abstract, poster, demonstration, sales catalog, news release, internal memorandum, oral presentation, or discussion with an industry representative, offer of samples, or a sale. SPECIFY DATE AND ATTACH COPIES OF PROPOSED WRITTEN DISCLOSURE.

Future disclosure of the above invention will likely be through patents, manuscripts, thesis, and oral presentations. DeSimone plans to present these concepts to DuPont on February 16, 2004

- d. Describe any other factors that might influence the decision whether or not and when to file a patent application, e.g., past or future public use of the invention, disclosure, or the likelihood that similar technology may be developed elsewhere.

6. SPONSORSHIP FOR WORK LEADING TO THE INVENTION: (this includes industry, foundation and state or federal sponsorship. If there is no sponsorship, type "none" in the sponsor field.)

- a. Name of sponsor(s): Kenan Professorship 660829

OTD 04.06.07

Complete sponsor contract/grant number(s): _____ UNC-CH Acct. Number: _____
 Funding period: _____
 Principal Investigator(s): _____

- b. Please list **any** encumbrances or obligations affecting this invention due to a Material Transfer Agreement, receipt of equipment or supplies, or other obligations.

OTD _____
CONFIDENTIAL

7. PROSPECTS FOR COMMERCIALIZATION:

- a. Indicate any apparent commercial interest. Please name companies and specific persons if possible.

Fluidigm (Stephen Quake)
 Caliper (Michael Ramsey)
 CTI

- b. List names of other qualified firms that make comparable equipment or products, with your comments, if any.

Fluidigm
 Caliper
 CTI

8. CONFLICT OF INTEREST INFORMATION: (use extra sheets as needed)

- a. Do any of the disclosing parties serve as either a director, officer, or board member of the company or companies named in 6 or 7 above? If so, please list in what capacity each person serves.
- b. Do any of the disclosing parties consult for any of these companies? If so, please list the company(ies) for which each consults.
- c. Do any of the disclosing parties hold a financial interest in any of the companies? If so, please list the company(ies) in which financial interest is held.

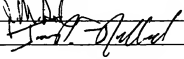
[Use the space below and additional sheets to elaborate on answers to questions and to provide any other helpful information.]

OTD C4-0067

V. PFPE networks as gas separation membranes


The chemical nature of these functionalized PFPE materials make them ideal candidates for gas separation membranes for CO₂, methane, hydrogen, CO, CFCs, CFC alternatives, organics, nitrogen, methane, H₂S, amines, fluorocarbons, fluoroolefins, O₂, water purification and others. These membranes may be stand alone films, composite films, or contain co-monomers incorporated therein to finely tune the permeability properties. The mechanical strength and durability of such membranes can be finely tuned by adding composite fillers such as silica particles and others.

CONFIDENTIAL**Signatur (s) of Disclosing Party(ies):**

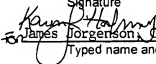

 date 2/10/04
 date 2/10/04
 date _____
 date _____
 date _____
 date _____

Signature of Person Witnessing This Disclosure: [This should be a non-discloser with the technical expertise to understand the invention.]

The undersigned has read and understands this Report of Invention:


 2-10-04
 Signature _____ date _____
 Charles Jones, Graduate
 Typed name and title

Signature of Department Chairperson(s) Affected by this Disclosure*:

2-10-04
 Signature _____ date _____

 James Jorgerson, Chairman
 Typed name and title

Signature _____ date _____
 Typed name and title

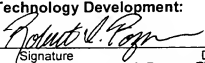
Signature _____ date _____
 Typed name and title

Signature _____ date _____
 Typed name and title

* By signing in the appropriate space, the Department Chairperson(s) is indicating only that he/she has seen and reviewed this Report of Invention.

PLEASE SEND THIS FORM TO: OFFICE OF TECHNOLOGY DEVELOPMENT, CB# 4105, 308 BYNUM HALL. Phone--966-3929, FAX--962-0646.

Office of Technology Development:


 2/10/04
 Signature _____ Date disclosure received by Office of Technology Development
 Robert I. Pozner, Ph.D.
 Senior Associate Director
 Typed name and title